Appendix A: A copy of the Pending Claims

56. (Amended) A substrate for analyzing a nucleic acid, the substrate comprising:

a cavitated fiber optic wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100 μm, the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and 5.0 mm in thickness; and wherein the depth of each well ranges from between one half the diameter of an individual optical fiber to three times the diameter of an individual optical fiber;

a plurality of beads within the cavitated wafer, wherein each bead has a pyrophosphate sequencing reagent attached thereto.

57. The substrate of claim 56, wherein the nucleic acid sequence is an anchor primer.

58. The substrate of claim 56, wherein the substrate comprises a plurality of fiber optic surfaces.

59. The substrate of claim 58, wherein the fiber optic surface includes two or more anchoring primers separated by approximately 10 um to approximately 200 um.

60. The substrate of claim 58, wherein the fiber optic surface includes two or more anchoring primers separated by approximately 10 um to approximately 150 um.

61. The substrate of claim 58, wherein the fiber optic surface includes two or more anchoring primers separated by approximately 150 um.

62. The substrate of claim 58, wherein the fiber optic surface includes two or more anchoring pads separated by approximately 10 um to approximately 150 um.

63. The substrate of claim 62, wherein the surface area of each pad is approximately 10 um2.

64. (Amended) The substrate of claim 56 wherein the wafer further comprises 10^3 or more groups of oligonucleotides in said wells.

65. The substrate of claim 64, wherein said substrate comprises 10^4 or more different groups of sequences in discrete known regions.

66. The substrate of claim 64, wherein said substrate comprises 10^5 or more different groups of oligonucleotides with known sequences in discrete known regions.

67. The substrate of claim 64, wherein the groups of oligonucleotides are attached to the surface by a linker.

68. The substrate of claim 64, wherein the groups of oligonucleotides are covalently attached to the surface.

69. (Amended) An array of more than 1,000 different groups of oligonucleotide molecules, a cavitated fiber optic wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100 μm, the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and 5.0 mm in thickness; and wherein the depth of each well ranges from between one half the diameter of an individual optical fiber to three times the diameter of an individual optical fiber.

70. The array of claim 69, wherein said area is less than 10,000 microns2.

72. The array of claim 69, wherein said array comprises more than 10,000 groups of oligonucleotides of known sequences.

73. An apparatus for analyzing a nucleic acid sequence, the apparatus comprising:

a reagent delivery chamber, wherein the chamber includes a substrate with immobilized nucleic acids;

a conduit in communication with the reagent delivery chamber;

an imaging system in communication with the reagent delivery chamber; and

a data collection system in communication with the imaging system.

74. The apparatus of claim 73, wherein the substrate is a planar substrate.

75. The apparatus of claim 73, wherein the substrate is a cavitated planar substrate.

76. The apparatus of claim 73, wherein the imaging system is a fiber optic system.

77. The apparatus of claim 73, wherein the substrate comprises

a cavitated fiber optic surface in communication with said imaging system; and a nucleic acid sequence linked to the fiber optic surface.

78. The apparatus of claim 77, wherein the substrate comprises a plurality of fiber optic surfaces, said fiber optic surfaces being in communication with said imaging system.

79. The apparatus of claim 78, wherein the fiber optic surfaces include two or more anchoring primers separated by approximately 100 um to approximately 150 um.

80. The apparatus of claim 78, wherein the fiber optic surfaces include two or more anchoring primers separated by approximately 150 um.

81. The apparatus of claim 78, wherein the fiber optic surfaces include two or more anchor pads separated by approximately 100 um to approximately 150 um.

82. The apparatus of claim 78, wherein the surface area of each pad is approximately 5um2 to approximately 10,000 um2.

83. The apparatus of claim 78, wherein the surface area of each pad is approximately 10 um2.

84. (Amended) An apparatus for processing a plurality of nucleic acids, the apparatus comprising:

a flow chamber having disposed therein a cavitated fiber optic wafer surface

a cavitated fiber optic wafer formed from a fused bundle of a plurality of individual optical fibers, each individual optical fiber having a diameter between 3 and 100 μm, the wafer comprising a top surface and a bottom surface, the top surface comprising at least 10,000 wells, wherein said wells are etched into the top surface of the cavitated fiber optic wafer and wherein the thickness of the wafer between the top surface and the bottom surface is between 0.5 mm and 5.0 mm in thickness; and wherein the depth of each well ranges from between one half the diameter of an individual optical fiber to three times the diameter of an individual optical fiber;

a plurality of beads within the cavitated wafer, wherein each bead has a pyrophosphate sequencing reagent attached thereto;

fluid means for delivering pyrosequencing reagents from one or more reservoirs to the flow chamber so nucleic acids disposed in the wells of the fiber optic wafer are exposed to the reagents; and

detection means for detecting optical signals from each well, wherein said detection means is in communication with the wells, each optical signal being indicative of reaction of the pyrosequencing reagents with the nucleic acid in a well.

85. The apparatus of claim 85, wherein said detection means further comprises signal tracking means for correlating said optical signals from each of said

microparticles in each of said digital images to form for each said microparticle of said plurality a sequence of said optical signals.

86. (Amended) The apparatus of claim 85, wherein said detection means is a CCD camera.

87. The apparatus of claim 86, wherein said analyte is DNA.

88. (New) The substrate of claim 56 wherein the substrate has a polished fiber optic surface opposite to the cavitated fiber optic surface.

89. (New) The substrate of claim 88 wherein the polished surface allows for optical coupling to a second optical fiber.

90. (New) The substrate of claim 56 wherein the cavitated surface is coated.

91. (New) The substrate of claim 90 wherein the coating is selected from the group consisting of plastic, gold layers, organosilane reagents, photoreactive linkers, hydrophilic polymer gels and pluronic polymers.

92. (New) The substrate of claim 56 wherein said sequencing reagent is luciferase.

93. (New) The substrate of claim 56 wherein said sequencing reagent is sulfurylase.

94. (New) The array of claim 69 wherein the wafer has a polished fiber optic surface opposite to the cavitated surface.

95. (New) The array of claim 94 wherein the polished surface allows for optical coupling to a second optical fiber.

96. (New) The array of claim 69 wherein the cavitated surface is coated.

97. (New) The array of claim 96 wherein the coating is selected from the group consisting of plastic, gold layers, organosilane reagents, photoreactive linkers, hydrophilic polymer gels and pluronic polymers.

98. (New) The array of claim 69 wherein said sequencing reagent is luciferase.

99. (New) The array of claim 69 wherein said sequencing reagent is sulfurylase.